

REMARKS

Claims 1-51 and claims 56-59 are pending. Claims 1, 4-6, 15, 33, 36, 44, 45, 47, 49, 50, and 56-59 have been amended. Claims 7-14, 16-19, 23-32, 34-35, 39-42, and 46 have been cancelled without prejudice. Claims 52-55 have been withdrawn by the Examiner [Office Action, page 3, third full paragraph].

Applicants acknowledge election without traverse of Group II, claims 1-60 drawn to compounds and methods of use wherein G or W is a directly linked piperazinyl or morpholinyl group. As a result of the above claim cancellations and withdrawals, the following claims are now pending: compound and composition claims 1-6, 15, 20-22, 33, 36-38, 43-45, and 47-48, and method claims 50-51 and 56-59.

In addition to changing the dependencies of certain claims, the amendments include the following.

Claim 1 was amended to exclude non-elected subject matter. Support for adding the terms "piperazinyl or morpholinyl" in the definition of W can be found in original claim 1, where W can be a C 1-8 heterocyclyl, and the specification on page 11, line 33 and page 12, line 3.

Claims 4-6 were amended to replace "G" with -W-; support can be found in original claim 1, where one of R1, R2, and R3 is G or W. Similarly, claim 15 was amended to replace "Q" with -W-.

Claims 44 and 45 were amended by deleting compounds not within the elected subject matter.

Claims 47, 49, and 50 were amended to change the dependencies.

Claims 51 and 58 were amended to delete "(predementia)" with the understanding that mild cognitive impairment includes predementia.

Applicants respectfully request reconsideration of the pending claims in view of the above amendments and remarks below.

Objection

Claims 1-51 and 56-59 were objected to for containing non-elected subject matter [Office Action, page 3, fourth full paragraph]. Applicants have cancelled claims 7-14, 16-19, 23-32, 34, 35, 39-42, and 46 without prejudice and amended claims 1, 4-6, 15, 33, 36, 44, 45, 47, 49, 50, and 56-59 to overcome this objection.

Claims 47-49 and 56-59, now amended to overcome the above objection, had no other statutory or art-based rejections and are therefore believed to be in condition for allowance.

Rejection Under 35 USC 112

Claims 59, 51, and 50 were variously rejected.

Claim 59 was rejected for lack of enablement because "applicant does not give support for 'preventing' all forms of these disorders" (such as upper airway allergic response, nasal congestion, or allergic rhinitis) [Office Action, page 6, second paragraph]. This rejection is respectfully traversed.

While Applicants recognize that, in general, "prevention" of a disease may be more difficult to demonstrate or to believe than "treatment" of a disease, Applicants nevertheless request reconsideration for the following simple reason.

It is common practice for people with allergies or hayfever to take an antihistamine in the morning or evening. The intent and the usual result is that, for the next several hours, they will be less congested or be able to breathe more easily. In other words, congestion is prevented. It is true that commercial antihistamines may relate to a different histamine subtype than that related to the instant application. However, the point is that the kinds of congestion in claim 59 are known to be susceptible of prevention, and that such a utility is therefore not incredible on its face. (This would be in contrast, for example, to a disease such as cancer, with multiple and inter-related causes and long time delays between exposure to a carcinogen and the perceptible occurrence of a tumor, and no known preventive therapy.) Applicants respectfully submit that the data presented in the application is sufficient to support the H3 antagonism activity of the claimed compounds, and therefore supports the method of preventing upper airway allergic response, nasal congestion, or allergic rhinitis, as claimed.

As claim 59 had no other statutory or art-based rejections, Applicants respectfully submit that claim 59 is in condition for allowance.

Claim 50 was rejected for indefiniteness because the term "modulate" was used. According to the Examiner, " 'Modulate' means that a histamine H3 receptor can both inhibit and cause a disease or condition. It is unclear whether Applicant claims that the role of histamine H3 is to inhibit or to cause a disease or condition." [Office Action, page 7, second full paragraph].

To clarify, Applicants claim methods of treating an undesirable disease or condition. Applicants do not claim methods of causing undesirable diseases or conditions. The compounds of the application have been shown to modulate histamine H3 receptor, and therefore are suitable for treating disease or conditions that are affected by modulation of the histamine H3 receptor.

As claim 50 had no other statutory or art-based rejections, Applicants respectfully submit that claim 50 is in condition for allowance.

Claim 51 was rejected for indefiniteness because both "mild cognitive impairment" and "predementia" were used in a Markush group, and according to the Office Action, predementia is a narrower statement of mild cognitive impairment. Applicants have amended claim 51 and also claim 58 where similar language appears in a similar context, to delete "predementia" solely on

the basis that mild cognitive impairment is understood to include prementia.

As claim 51 had no other statutory or art-based rejections, Applicants respectfully submit that claim 51 is in condition for allowance.

In view of the remarks and amendments above, Applicants respectfully request that these 112 rejections of claims 50, 51, and 59 be withdrawn, and that these claims be allowed.

Rejection Under 35 USC 103

Claims 1-46 were rejected as unpatentable over Goto et al. (CAPLUS AN 1996:754425) in view of Greene ("Protective Groups in Organic Synthesis") [Office Action, page 4, last paragraph].

According to the Office Action, "the difference between Goto et al. and the instant claims is that Goto et al disclose an acyl protecting group on the nitrogen of the piperidine ring, while the instant claims consist of a (phenyl)C 1-6 alkyl protecting group on the nitrogen of the piperidine ring [Office Action, page 5, second paragraph]." According to the Office Action, one of ordinary skill would have been motivated to use Goto to prepare the claimed compounds because the substitution of a phenylalkyl nitrogen protecting group for an acyl nitrogen protecting group is an obvious variant [Office Action, page 5, third paragraph]. Applicants respectfully traverse this rejection.

It is not proper to combine Goto with Greene. On the one hand, Greene is a reference for chemical synthesis, a reference for chemical protecting groups. On the other hand, Goto is a reference about antioxidants, about compounds that inhibit degeneration and necrocytosis of cerebral nerve cells [Goto, claim 1, column 52]. If Applicants were claiming a chemical process, then it might be proper to cite Greene, since the chemical synthetic similarity of one protecting group with another would be relevant in a given chemical process. However, this is not the subject matter that Applicants are claiming.

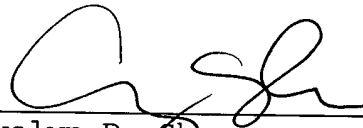
Applicants are claiming compounds and methods of using them to treat histamine H3 receptor-mediated conditions and diseases. Nothing in Green or Goto suggests that the inhibition of degeneration and necrocytosis of nerve cells is in any way related to histamine H3 receptor. Nothing in Greene or Goto suggests that a putative similarity in chemical protecting groups is in any way related to the efficacy of Goto's compounds as necrocytotic inhibitors. The Office Action has not pointed out where to find the suggestion in Greene or Goto that, in view of the structural differences between Goto and the claimed compounds, one of ordinary skill would have a reasonable expectation of both making the structural changes described in the Office Action and succeeding in obtaining a good inhibitor of degeneration and necrocystosis.

The Office Action has failed to state a prima facie case of obviousness. It is improper to combine Goto with Greene. Even if they were combined, the combination does not provide the required rationale or teaching.

For the reasons stated above, Applicants respectfully request that this rejection be withdrawn.

Applicants respectfully petition that the period for response be extended three months up to and including November 22, 2002. Please charge any fees to Deposit Account number 10-0750/ORT-1474/EDS. Three copies of this request are enclosed herewith.

Respectfully submitted,



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